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| APPLICATION NO.   | FILING DATE | FIRST NAMED INVENTOR    | ATTORNEY DOCKET NO.         | CONFIRMATION NO. |
|---|-------------|-------------------------|-----------------------------|------------------|
| 10/614,603  | 07/07/2003  | Kenneth Dawson Bagshawe | 20747/82<br>(AEPW/P16819US) | 7800             |
| 7590 04/22/2004   |             |                         | EXAMINER                    |                  |
| Nixon Peabody LLP<br>Clinton Square<br>P.O. Box 31051<br>Rochester, NY 14603-1051 |             |                         | SHAHNAN SHAH, KHATOL S      |                  |
|   |             |                         | ART UNIT                    | PAPER NUMBER     |
|   |             |                         | 1645                        |                  |

DATE MAILED: 04/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary****Application No.**

10/614,603

**Applicant(s)**

BAGSHAW ET AL.

**Examiner**

Khatol S Shahn-Shah

**Art Unit**

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 07 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-6 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☒ Certified copies of the priority documents have been received in Application No. 09/091933.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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***DETAILED ACTION***

1. Applicants' preliminary amendment of 7/7/2003 is acknowledged. Specification pages 1, 3, 26 and 27 have been amended. Priority statement and brief description of drawings have been added to the specification.
2. Claims 1-6 are pending and under consideration.

***Abstract***

3. Abstract of disclosure has been received on 7/7/2003. The abstract is proper and has been approved by the examiner.

***Drawings***

4. Revised copy of figure 2 was received on 7/7/2003. These drawings are informal. The informal drawings filed in this application are acceptable for examination purposes. When the application is allowed, applicant will be required to submit new formal drawings. In unusual circumstances, the formal drawings from the abandoned parent application may be transferred by the grant of a petition under 37 CFR 1.182.

***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

6. Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 6 recite, "an antibody or fragment or derivatives thereof". It is unclear what constitute these fragments as well as the derivatives. Furthermore, it is unclear if the derivative

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has 100% homology to the full length, or if the limitation of being a derivative would include substitutions, deletions and additions to said antibody.

The term "substantially" in claims 1 and 6 is a relative term, which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

It is not clear what applicants intend in reciting the term "capable" in claims 1 and 6.

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Connors et al. (WO 95/12678) in view of Blakey et al. (Cell Biophysics Vol. 24/25, pp. 175-183, 1994) and further in view of Siegall et al. (Bioconjugate Chemistry Vol. 3, pp. 302-307, 1992).

The claims are drawn to a therapeutic system for destroying a target cell within a host. Connors et al. teach a system comprising a prodrug and a viral vector encoding an enzyme (nitroreductase) which converts said prodrug into a cytotoxic drug (see claim 1). Connors et al. teach said nitroreductase requires NADH or NADPH as a cofactor (see page 5). Connors et al. teach that the prodrug is CB1954 (see page 8). Connors et al. teach that the nitroreductase is dependent upon cofactor found in cells (see column 13, last paragraph, continued on next page).

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Connors et al. teach that the viral vector encoding nitroreductase can be delivered into a cell using an antibody that is internalized (see page 19). Connors et al. teach that administered viral vector leads to the production of nitroreductase inside a target cell wherein administered prodrug is then converted to a cytotoxic drug (see abstract). Connors et al. do not teach that the nitroreductase itself is introduced into a target cell. However Blakey et al. teach that antibody-enzyme conjugates wherein the antibody portion of the conjugate mediates internalization can be used in ADEPT systems if the prodrug in said system can be internalized (see page 182, last sentence and page 183). The system used by Connors et al. uses a prodrug that can be internalized. Connors et al. Do not teach BR96 antibody. However, Siegall et al. teach the BR96 antibody was used in an immunoconjugate wherein said antibody mediated internalization of said conjugate (see abstract). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Connors et al. teach that exogenous nitroreductase introduced into a target cell can convert a prodrug into a cytotoxic drug and that an antibody capable of internalization can be used to introduce exogenous molecules into a cell, while Blakey et al. teach that antibody-enzyme conjugates wherein the conjugate is internalized can be used in ADPT systems if the prodrug used in said system can be internalized. One of ordinary skill in the art would have been motivated to do the aforementioned because Connors et al. teach that exogenous nitroreductase introduced into a cell will only convert prodrug into cytotoxic drug inside cell because the required cofactor is found inside cells and not found free in the blood stream (see pages 13 and 14). While Siegall et al. teach that the BR96 antibody was used in an immunoconjugate wherein said antibody mediated internalization of said conjugate.

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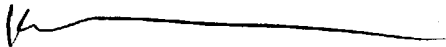
*Conclusion*

9. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol S Shahnian-Shah whose telephone number is (571)-272-0863. The examiner can normally be reached on 7:30am-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith can be reached on (571)-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

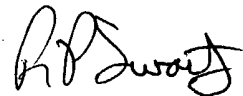


Khatol Shahnian-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

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April 17, 2004



RODNEY P SWARTZ, PH.D  
PRIMARY EXAMINER